neurological examination at the time of the decreased visual acuity. The following patients were excluded: (1) 21 (18%) because signs and symptoms indicative for multiple sclerosis were already present, (2) 14 (12%) without VER abnormalities (5/14 turned out to be hysteric) and (3) 19 (16%) with insufficient clinical data. The remaining 64 patients all had a history of rapidly progressive visual loss, in combination with painful eyemovements (72%), a central or paracentral scotoma (81%) and a delayed, decreased or absent P100 amplitude on pattern reversal, visual evoked response (VER) recording (100%).

During follow up period another 16 out of the 64 patients had to be excluded because the suspicion of intoxication (3), Leber's disease (2), vascular occlusion (3), Devic's disease (1), tumour compression of the optic nerve (4) or refractive disorder (3).

The remaining 48 patients all had a partly or complete recovery of the visual acuity within 4 weeks to 9 months. The follow up period of these patients varied from 6 months to 3-5 years. They all were re-examined neurologically in 1986–87.

During follow up four patients had a relapse of the optic neuritis (ipsilateral 1, contralateral 3). These four patients all had other neurological symptoms besides the decreased visual acuity at the time of this investigation. Another 25 developed signs and symptoms indicative for multiple sclerosis, such as paraesthesiae 14, sensory loss 8, impotence 2, bladder dysfunction 5, pyramidal syndromes 2, ataxia 3, diplopia 3. Mostly these signs and symptoms were found in mutual combination.

The total percentage of multiple sclerosis after optic neuritis within a period varying from 6 months to 3-5 years was 60% (29/48) which is rather high incidence compared with other studies, which were mostly concerned with longer periods of follow up.

The conclusion from this study is that VER recording in combination with case history and campimetry are able to select those optic neuritis patients who have a high risk for developing multiple sclerosis in the near future. The selection of the optic neuritis patients on the basis of VER and physical examination does give a higher certainty for the developing of multiple sclerosis than any other auxiliary diagnostic method, including lumbar puncture, and HLA typing or clinical examination alone.

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No viral antigens detected in brain tissue from a case of acute encephalitis lethargica and another case of post-encephalitic Parkinsonism

Sir: The case of encephalitis lethargica is unknown. At the time of the 1915–1930 pandemic, it was suggested that a virus was responsible. In fact, in 1920 when Levaditi and Harvier isolated herpes virus from the brain of a patient who died of the disease, they claimed that virus to be its cause. While a progressive Parkinsonism was a frequent sequel of encephalitis lethargica, sporadic and usually transitory Parkinsonian syndromes have continued to be reported in association with established viruses such as Japanese B encephalitis, Western equine encephalitis, central European tick-borne encephalitis, coxsackie group B and lymphocytic choriomeningitis viruses.

The fact that the clinical and pathological features of encephalitis lethargica strongly suggested a viral etiology, plus the unquestionable association of certain cases of postencephalitic Parkinsonism with conventional viruses, have sustained a continued interest in the possible connection between encephalitis lethargica, including postencephalitic Parkinsonism, and a virus. Two relatively recent studies address this point: Rail et al described eight cases which conformed to the diagnosis of encephalitis lethargica, of which six presented between 1960 and 1980; serum and CSF from three of the patients were tested for antibodies against a number of viruses including influenza A and B, parainfluenza, adenoviruses, measles, mumps, herpes and varicella-zoster, with negative results. Esiri and Swash tested midbrain sections from a patient who died of encephalitis lethargica in 1920 during the acute phase (day 7) of the illness with an antiserum against herpes virus antibody by the immunoperoxidase technique; the reaction was negative for herpes antigen.

We report here the result of attempts to detect virus antigens in brain sections from the Esiri and Swash case (London Hospital case 15/20); and from one of the Rail et al cases (No 7 BW 34520) who presented with oculargic crises in 1965, developed Parkinsonism shortly after, and died in 1981.

Coronal sections of frontal cortex, temporal cortex, substantia innominata, midbrain at the level of the superior colliculus (including the substantia nigra) and at the level of the rostral end of the 4th ventricle (at the location of the locus ceruleus), were first examined after staining with haematoxylin-eosin, silver (Naoumenko-Feigin) and thioflavin S, in order to determine the nature, extent and intensity of the lesions. Haematoxylin-eosin sections of the 1920 acute case of encephalitis lethargica showed pronounced disruption and destruction of the few remaining melanin-containing neurons in the substantia nigra and locus ceruleus; very marked and widespread vascular cuffing with as many as six to eight layers of small mononuclear cells predominately lymphocytic; large number of lymphocytic nodules and abundant astrocytes in both midbrain sections. The 1981 case showed much less generalised reaction but again, the remaining melanin-containing neurons in both substantia nigra and locus ceruleus were markedly reduced. No amyloid plaques or neurofibrillary tangles were detected in any of the sections stained with thioflavin S. The silver stain detected rare plaques or tangles in the 1920 case and only occasional plaques or tangles in the lateral case. Confirmation of the astrocytic reaction in the substantia nigra sections in both cases was sought by means of the immunoperoxidase test using an antisem against glial fibrillary acidic protein; the astrocytic reaction observed in the acute case was exceedingly intense particularly in the plexi-
form layer of the superior colliculus and periaqueductal area, somewhat less in the substantia nigra. The astrocytosis in the 1981 case was clearly visible in the same areas but much less marked than in the 1920 case.

Since our histological observations showed marked lesions only in the midbrain sections, our subsequent immunocytochemical studies were confined to these areas. Attempts to find antigens from several viruses were carried out by means of immunoperoxidase techniques using antisera against the following viruses or strains: Influenza A, strains A-2 Japan 305/57, WS/33 and A-swine 1976/31, prepared in chicken; A/New Jersey, prepared in goat; and neuroadapted NWS strain prepared in rabbit. Influenza B, strain Hong Kong, prepared in goat, herpes virus type 1, prepared in rabbit, rubella and cytomegalovirus, prepared in goat, measles and mumps viruses, prepared in guinea pig. The tests were indirect immunoperoxidase with the chicken sera, and peroxidase-antiperoxidase (PAP) with rabbit, goat and guinea pig sera.

The peroxidase tests were uniformly negative; no antigen for any of the above listed viruses or strains were detected in any of the sections examined. These results confirm the absence of herpes virus antigen in the 1920 Esiri and Swash case; and do not support previous observations by Gamboa et al using a different technique, direct immunofluorescence and frozen sections, who reported positive reactions with NWS strain of influenza A antiserum. Furthermore, our results have added cytomegalovirus, rubella, mumps and measles, all widespread conventional viruses, to the list of viruses whose antigens have not been detected in brain tissue from cases of encephalitis lethargica and post-encephalitic Parkinsonism.

All attempts have thus far failed to show a reproducible connection between a known virus and encephalitis lethargica or post-encephalitic Parkinsonism. However, the nature of the histological lesions in the present cases still strongly suggest a viral aetiology. Our negative immunocytochemical results may be due to the fact that the procedures used for antigen detection were not sensitive enough; or that the responsible virus, established or as yet undiscovered, was not among those used as probes; or that the specimens investigated were taken at a time when the antigen had already been degraded or eliminated; or, of course, that no virus is involved. It is interesting to note that in a similar disease, idiopathic Parkinson's disease, McGeer et al recently found evidence of an active neuropathological process at the time of death, from which they concluded that a chronic infection or an autoimmune process following an infection was a tenable hypothesis.

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References

Head injury induced migraine coma simulating acute extradural intracranial haemorrhage

Sir: Migraine induced by head trauma and migraine coma are uncommon but well described. We present a case in which both conditions coincided, simulating the presentation of acute extradural haemorrhage.

A 15 year old girl suffered a blow to the nose while playing hockey. She had visual attacks occurring after the blow which simulated acute extradural intracranial haemorrhage. She had a history of classic migraine over the previous year. Her aura consisted of teichopsia, which took exactly the same pattern as both the episodes of scintillation which followed her head injury, light-headedness, nausea and drowsiness, and was identical to the prodrome of her present illness. The headache was mild and often brief, accompanied by photophobia. There was no past history of her migraine following head injury. She had a family history of migraine.

Electroencephalography the day after admission was normal, as was cerebrospinal fluid examination (including immunoglobulins) on the 7th day after admission. At 5 days her monoparesis was just detectable, and she still had mild impairment of digit span. At 8 days she was completely recovered.

The patient had a typical history of classical migraine. The present episode was preceded by symptoms identical in detail to her usual aura, confirming its migrainous nature. The normal CT, EEG and CSF studies, and her complete recovery excluded serious illness. The connection with head injury is strongly supported by the time course of her illness, and the fact that even those scintillations occurring immediately after the blow were identical to her usual migrainous teichopsia.

Secondary depression of conscious level short of coma may occur without migrainous features following head injury and migrainous attacks precipitated by minor head injury may be accompanied by drowsiness, particularly in children. The only reports of coma with clear features of migraine are of one family in which migraine coma, often precipitated by trivial head trauma, was associated with dominantly inherited cerebellar ataxia and of one sporadic case similar to our own.

In patients with trauma-induced migraine a head injury that would otherwise have only minor or subclinical effects can precipitate a migraine attack. The reticular formation of the brainstem is thought to be important in

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